IN THE CLAIMS:

Please enter the following rewritten claims:

11. (Amended) A method for determining in a proteomic mixture the presence of active target members of a group of related proteins, said related proteins related in having a common functionality for conjugation at an active site, said method comprising:

combining a first portion of said proteomic mixture with at least one activity-based probe comprising a reactive functionality specific for said active site when active, under conditions for conjugation of said probe to said target members;

combining a second portion of said proteomic mixture that has been subjected to non-specific inactivation with said probe(s) under the same conditions used with said first portion of said proteomic mixture;

determining the presence of target members conjugated with said probe(s) in each of said first and second portions of proteomic mixtures; whereby the presence of a greater amount of target members conjugated to said probe(s) in said first portion of said proteomic mixture than in said second, inactivated portion of said proteomic mixture indicates the presence of an active target member.

B16

12. (Amended) A method according to Claim 11, comprising the additional step of characterizing said active target members conjugated with said probe(s).

13. (Amended) A method according to Claim 12, wherein said characterizing comprises degrading said active target member and determining the resulting fractions by mass spectrometry.

14. (Amended) A method according to Claim 11, employing a plurality of activity-based probes having different reactive functionalities specific for different groups of related proteins.

15. (Amended) a method according to Claim 11, wherein said activity-based probe(s) comprises a detectable label.

16. (Amended) A method according to Claim 11, wherein said proteomic mixture is in an intact cell.

17. (Amended) A method for determining in a plurality of proteomic mixtures the presence of active target members of a group of related proteins in each of said proteomic mixtures, said related proteins related in having a common functionality for conjugation at an active site, said method comprising:

combining each of said proteomic mixtures with at least one activity-based probe comprising a reactive functionality specific for said active site when active, under conditions for conjugation of said probe(s) to said target members;

determining the presence of target members conjugated with said probe in each of said proteomic mixtures;

B16 Con'd

whereby the presence of said target members conjugated to said probe(s) in said proteomic mixtures is indicative of the presence of active target members in said mixtures.

18. (Amended) A method for determining in a plurality of proteomic mixtures the presence of active target members of a group of related proteins, said related proteins related in having a common functionality for conjugation at an active site, said method comprising: :

combining a first portion of each of said proteomic mixtures with at least one activity-based probe comprising a reactive functionality specific for said active site when active, under conditions for conjugation of said probe(s) to said target members;

combining a second portion of each of said proteomic mixture that has been subjected to non-specific deactivation, with said probe(s) under the same conditions used with said first portion of said proteomic mixture; and

determining the presence of target members conjugated with said probe(s) in each of said first and second portions of said proteomic mixtures;

whereby the presence of a greater amount of target members conjugated to said probe(s) in said first portion of said proteomic mixtures than in said second, inactivated portion of said proteomic mixtures indicates the presence of active target members.

19. (Amended) A method for determining in a proteomic mixture the presence of active target members of a group of related enzymes, said related enzymes related in having a common functionality for conjugation at an active site, said method comprising:

combining a first portion of said proteomic mixture with at least one activity-based probe comprising a reactive functionality specific for said active site when active, under the same conditions for conjugation of said probe to said target members;

combining a second portion of said proteomic mixture that has been subjected to non-specific inactivation, with said probe(s) under the same conditions used with said first portion of said proteomic mixture;

Bio
Conic

determining the presence of target members conjugated with said probe(s) in each of said first and second portions of said proteomic mixture;

whereby the presence of a greater amount of target members conjugated to said probe(s) in said first portion of said proteomic mixture than in said second, inactivated portion of said proteomic mixture indicates the presence of an active target member.

20. (Amended) A method according to Claim 19, wherein said probe comprises a ligand and said determining is by binding said ligand in a conjugate to a support and isolating said conjugate.

21. (Amended) A method according to Claim 19, wherein said reactive functionality is a fluorophosphonate or fluorophosphoroate.

22. (Amended) A method according to Claim 19, wherein said active functionality is an α-haloketone.

23. (Amended) A method according to Claim 19, wherein said active functionality is sulfonate ester or epoxide.

24. (Amended) A method according to Claim 19, wherein said active functionality is a sulfonate ester.

B16 cnp

25. (Amended) A method according to Claim 19, wherein said active functionality is α-halohydroxamic acid.

26. (Amended) A method according to Claim 19, wherein said active functionality is an alkyne.

Please add the following new claims:

R-126

32 27. (New) A method according to Claim 17 or 18, comprising the additional step of characterizing said active target members conjugated with said probe(s).

R-126 B17 Rule 126

33 28. (New) A method according to Claim 27, wherein said characterizing comprises degrading said active target member and determining the resulting fractions by mass spectrometry.

34 29. (New) A method according to Claim 17 or 18, employing a plurality of activity-based probes having different reactive functionalities specific for different groups of related proteins.

35 30. (New) A method according to Claim 17 or 18, wherein said activity-based probe(s) comprises a detectable label.

36
31. (New) A method according to Claim 17 or 18, wherein said proteomic mixture is in an intact cell.

37
32. (New) A method according to Claim 17 or 18 further comprising the step of analyzing for the presence of proteins conjugated with said probe(s) using simultaneous individual capillary electrokinetic analysis or capillary HPLC.

38
33. (New) A method according to Claim 11, 17, 18 or 19 wherein said activity-based probe(s) are of the formula:

R* (F – L) -X

wherein:

X is a ligand for binding to a reciprocal receptor or a chemically reactive functionality for reacting with a reciprocal functionality to add a ligand;

L is a linking group;

F is a functional group reactive at an active site of a target enzyme; and

R is H or a moiety of less than 1kDal providing specific affinity for said target enzymes;

the * intends that R is a part of F or L.

39
34. (New) A method according to Claim 33, wherein F is a sulphonyl group and R is other than H and bonded to F.

40
35. (New) A method according to Claim 33, wherein F is a fluorophosphonyl or fluorophosphoryl group.

41
36. (New) A method according to Claim11, wherein at least one of L and X comprise at least one isotope in unnatural amount, and including the additional step of:

releasing at least a portion of said probe from said conjugate and identifying said portion by means of isotopic difference.

42
37. (New) A method according to any of Claims 11-13, 15-21, 27, 28, 30-33, 35 or 36 wherein said activity-based probe(s) are FP-biotin.

43
38. (New) A method according to any of Claims 11-13, 15-21, 27, 28, 30-33, 35 or 36 wherein said activity-based probe(s) are FP-peg-biotin.

44
39. (New) A method according to any of Claims 11-13, 15-20, 23, 24, 27, 28, 30-34 or 36 wherein said activity-based probe(s) are selected from the group consisting of Sulfonate 1 – Sulfonate 17.

45
40. (New) A method according to Claim 39 wherein said activity-based probe(s) are Sulfonate 15.

46
41. (New) A method according to Claim 14 or 29 wherein said activity-based probe(s) are selected from the group consisting of FP-biotin, FP-peg-biotin and Sulfonate 1 Sulfonate 17.

47
42. (New) A method according to Claim 21 wherein said group of related enzymes is serine hydrolases.

48
43. (New) A method according to Claim 22 wherein said group of related enzymes is cysteine hydrolases.

49
44. (New) A method according to Claim 23 wherein said group of related enzymes is related in having a common functionality comprising at least one of the following: cysteine, histidine, aspartate, and glutamate.

50
45. (New) A method according to Claim 24 wherein said group of related enzymes is alcohol dehydrogenases.